BIMM 124 Goals

Develop competency in understanding interactions between humans and infectious agents:

- bacteria
- viruses
- parasites

Develop

- **critical thinking skills**
- **analytical ability**

which may be applied to <u>any</u> infectious disease topics in future

Empower students to learn on their own.

Develop competence to evaluate **primary literature**.

Key components of BIMM 124 course design

- Reading in advance

- Mandatory sections

- Student groups (of 3)

- Lecture: use of clickers and peer instruction

- Write-ups on primary research papers

- Open-book exams

READING, prior to lecture

- Textbook
- Primary research literature … 10 papers per quarter

29 lectures

Blue indicates a lecture based upon primary literature.

Fall 2012

Intro to class
Intro to bacteria
Damage response
Immunity I
Immunity II
Immunity III
Immunity IV
Endogenous flora
Enteric bacteria
Enteric bacteria
Staphylococcus & Strep
Neisseria
Neisseria
Tuberculosis
Tuberculosis
Midterm
Helminths
Bad worms
Good worms
Intro to viruses
HIV
HIV
Influenza
Influenza
Alpha & Flaviviruses
Alpha & Flaviviruses
GI protozoal infections
Fungal infections
Malaria drug discovery

Fall 2013

Intro to class
Innate immunity I
Innate immunity II
Adaptive immunity I
Adaptive immunity II
Microbiota
Microbiota
Intro to bacteria
Secretory diarrhea
Secretory diarrhea
Chlamydia
Chlamydia
Staphylococcus
Staphylococcus
Drug development
Bacteria and dental hygiene
Helminths
Helminths as disease agents
Helminths alleviate autoimmune disease
Intro to viruses
Herpes
Herpes
HIV
HIV
Rotavirus
Rotavirus
Blood & tissue protozoa
Vaccines
Skype call to head of UNAIDS in Burkina Faso

READING, prior to lecture

- Textbook
- Primary research literature … 10 papers per quarter

Give students general guidelines and tips on reading (and studying) research papers at start of quarter.

Provide a sheet of tips for understanding each paper (explanation of cell lines, genes, techniques, jargon, etc).

If you do not understand the meaning of a word, LOOK IT UP!
If you do not understand a concept or technique, LOOK IT UP!

This is what scientists do. ☺

READING, prior to lecture

- Textbook
- Primary research literature … 10 papers per quarter

Come to class with a **prepared mind**.

Pre-lecture preview of course material
→ greater level of organization in a student's mind

Focus on comprehension, not memorization

Incentives to read:

- 3-question clicker quiz (Orange box questions)

Your likelihood of infection with *V. cholerae* is enhanced if:

a. you take antacids

b. you eat raw seafood

c. you have blood type O

d. you drink unboiled, unfiltered tap water in India

e. all the above

This study involved the use of:

a. human patients
b. live mice
c. guinea pigs
d. cell culture
e. b and d

READING, prior to lecture

- Textbook
- Primary research literature … 10 papers per quarter

Come to class with a **prepared mind**.

Pre-lecture preview of material
→ greater level of organization in a student's mind

Focus on comprehension, not memorization

Incentives to read:

- 3-question clicker quiz (Orange box questions)
- more challenging questions (Green box questions) involving group discussion
  (groups are called upon to respond to clicker questions)

CAPE comment:

Doing your reading is absolutely necessary for this class. You will be absolutely lost in lecture if you do not read the assignements beforehand.

Lecture: Peer instruction model

Pre-Class preparation

1) Presentation of a problem
2) Individual Thinking, Individual Vote

3) Group Discussion (with 2 other students)
- Practice discussing & analyzing challenging concepts
- Question the instructor or TA during discussion
- Reach group consensus

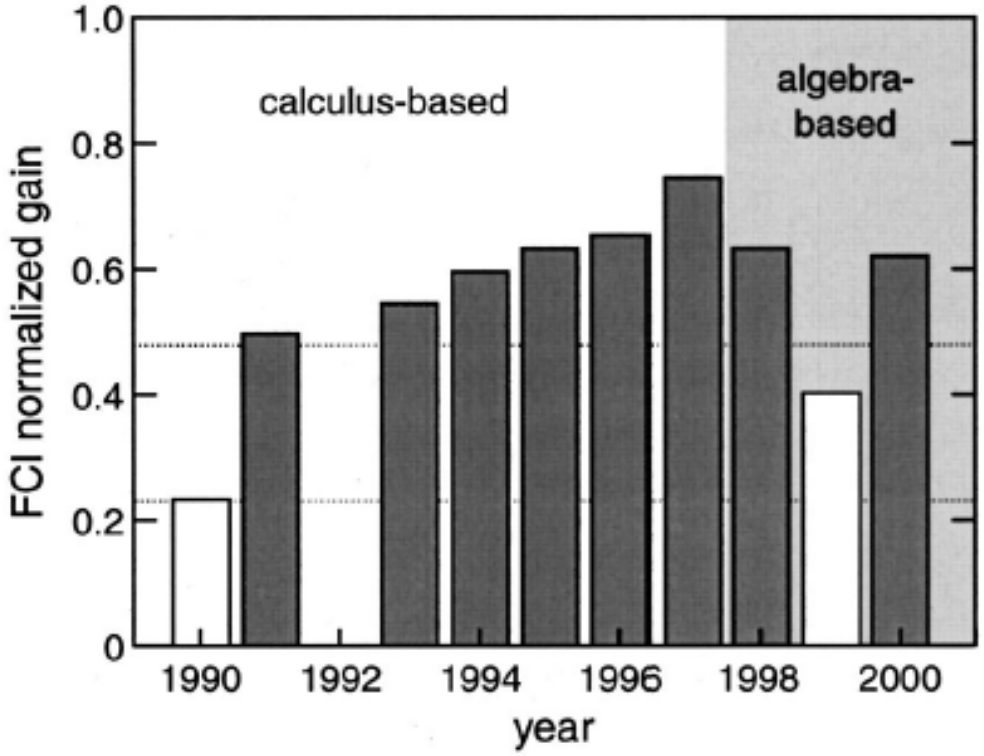
4) Vote again, according to group consensus

Class-wide discussion
(Instructor may call on specific groups to elaborate)
Explanation by instructor

Peer Instruction: Learning Gains in Physics Nearly Double

Traditional Instruction

Peer Instruction



Crouch, C., Mazur, E. (2001) Ten years of experience and results. American Journal of Physics. 69(9):970-977.

Benefits of Peer instruction Model

- active engagement in class (students don't "tune out")
- opportunity for student self-assessment
- opportunity for instructors to assess student understanding
- recognition of common misunderstandings
- practice application of basic principles to new problems
- preparation for exams

Chlamydia
Case study

Suzy Jones is a 18-year-old college student who presents to the Student Health Center seeking advice about contraception.

History

Has never had a pelvic exam.

Has had 2 sex partners in past 6 months

Does not use condoms or any other contraceptives

Her periods have been regular, but she has recently noted some spotting between periods.

Denies vaginal discharge, pain upon intercourse, genital lesions or sores

Physical exam

The genital exam reveals normal vulva, and vagina.

The cervix appears inflamed, bleeds easily, with a purulent discharge coming from the cervical os. "Endocervicitis"

No cervical motion pain, or uterine tenderness.

What microbiologic diagnosis should be presumed at the time of the exam?

a. *Chlamydophila pneumonia*
b. *Chlamydophila abortus*
c. *Chlamydia trachomatis*
d. *Neisseria gonorrhoeae*
e. c and d

What treatment is most appropriate while awaiting lab tests?

a. an intramuscular injection of vancomycin
b. oral azithromycin taken daily for 7 days
c. an intramuscular injection of ceftriaxone
d. no treatment … the infection usually clears without treatment
e. b and c

Which test(s) would NOT be used to confirm her diagnosis?

a. culturing a swab of the endocervix
b. microscopic examination of bacteria in the swab
c. detection of antigens from the swab using enzyme immunoassay
d. nucleic acid amplification (PCR) test on urine
e. All of these tests are potentially useful in this case.

If she had not come to the clinic, and the infection remained untreated, Suzy may have developed complications. Which of the following is NOT a complication of chronic *C. trachomatis* infection?

a. infection of infant if she gives birth
b. pelvic inflammatory disease
c. infertility
d. ectopic pregnancy
e. These are all potential complications.

Chlamydia Research paper

Chlamydial IFN-γ immune evasion is linked to host infection tropism

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Edited by Stanley Falkow, Stanford University, Stanford, CA, and approved June 9, 2005 (received for review May 20, 2005)

Chlamydiae are obligate intracellular pathogens that can exhibit a broad host range in infection tropism despite maintaining near genomic identity. Here, we have investigated the molecular basis for this unique host–pathogen relationship. We show that human and murine chlamydial infection tropism is linked to unique host and pathogen genes that have coevolved in response to host immunity. This intimate host–pathogen niche revolves around a restricted repertoire of host species-specific IFN-γ-mediated effector responses and chlamydial virulence factors capable of inhibiting these effector mechanisms. In human epithelial cells, IFN-γ induces indoleamine 2,3-dioxygenase expression that inhibits chlamydial growth by depleting host tryptophan pools. Human chlamydial strains, but not the mouse strain, avoid this response by the production of tryptophan synthase that rescues them from tryptophan starvation. Conversely, in murine epithelial cells IFN-γ induces expression of p47 GTPases, but not indoleamine 2,3-dioxygenase. One of these p47 GTPases (Igp1) was shown by small interfering RNA silencing experiments to specifically inhibit human strains, but not the mouse strain. Like human strains and their host cells, the murine strain has coevolved with its murine host by producing a large toxin possessing YopT homology, possibly to circumvent host GTPases. Collectively, our findings show chlamydial host infection tropism is determined by IFN-γ-mediated immunity.

immunity | virulence factors | pathogenesis | defense | coevolution

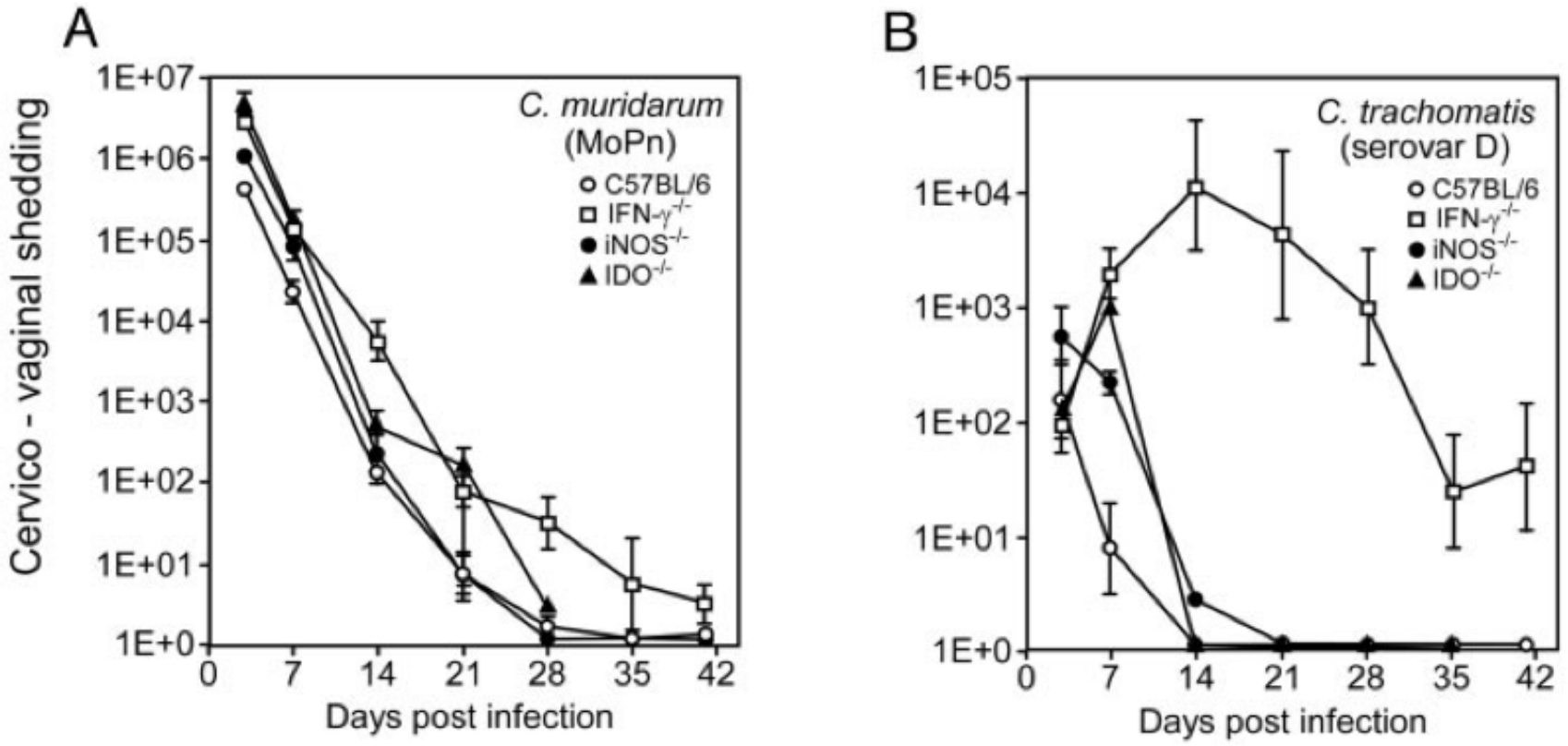
nonfusogenic with lysosomes; and (*ii*) targeting of the chlamydial vacuole to the perinuclear region where the organisms intercept essential lipids from the trans-Golgi exocytic pathway (8), the latter being unique to chlamydiae. Host factors capable of inhibiting these virulence mechanisms would be important in preventing chlamydial infection.

Despite their common cell biology, chlamydiae exhibit a broad spectrum in natural host infection tropism (9). This paradigm is most evident comparing *C. trachomatis* and *Chlamydia muridarum*, human- and mouse-specific pathogens, respectively. In their natural hosts, these strains are epithelial tropic and produce infections of the urogenital tract that result in similar pathology (10). Restriction in host tropism of human strains is overcome in IFN-γ-deficient mice (11), suggesting that tropism is linked to the immune response. The paradox of this host–pathogen relationship is that human and mouse strains share 99% gene content (12), indicating that a limited number of pathogen-specific virulence genes control evasion of IFN-γ-mediated host-specific defense mechanisms. Understanding these virulence factors and host defense mechanisms are logical goals toward defining better infection models for human strains.

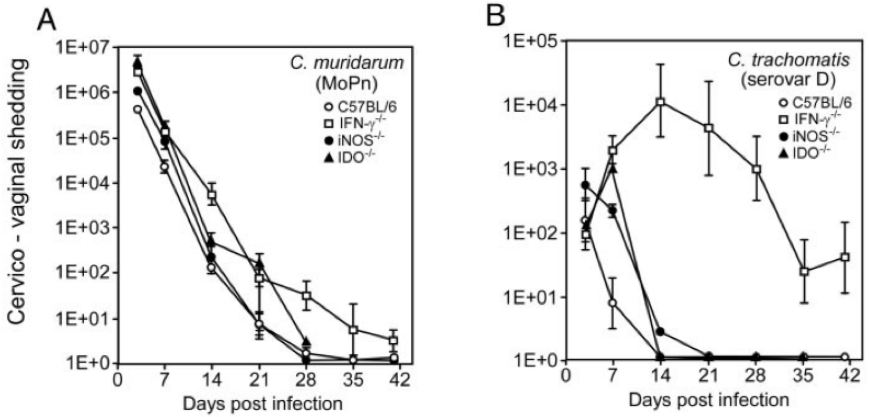
Here, we show that infection tropism of epithelial cells is strongly linked to a small subset of host-specific IFN-γ-mediated anti-chlamydial effector molecules and pathogen-specific virulence genes that interfere with these host defense mechanisms. Collectively, the data imply that murine and human chlamydial strains have coevolved with their respective mammalian hosts primarily to avoid IFN-γ-mediated defense mechanisms. The results suggest a

Figure 1

in vivo or *in vitro*?



What is indicated by these data?



a. Mouse chlamydia bacteria do not replicate effectively in wild-type mice.

b. Human chlamydia bacteria replicate prolifically in wild-type mice.

c. Mouse IFNγ inhibits the replication of human chlamydia in wild-type mice.

d. Mouse IDO is not induced by IFNγ in wild-type mice.

e. More than one

Optional write-ups on primary research papers

three assignments per quarter
optionally worth 8% of grade
(only 2 papers are necessary for full credit)

instructor provides each paper, a list of questions,
and perhaps tips to understand paper

students read paper
and hopefully discuss it with their group

students individually write up their answers

papers graded in section

Optional write-ups on primary research papers

2013 scores (up to 1 point per paper)

score	students	%
0	5	3%
0.5	2	1%
1	5	3%
1.5	6	4%
2	72	44%
2.5	26	16%
3	48	29%

89% got full credit (2 points)

45% did MORE than necessary for full credit
... value the practice

Mandatory write-up on primary research paper

one major paper per quarter
worth 30% of grade

students individually complete the assignment

Open-book exams

emphasize

- problem solving skills
- evaluation of case studies and research data
- extrapolation of basic principles to new situations

CAPE comment: *Be aware that you cannot cram for this class. The ability to quickly read and accurately analyze a biological/ medical research paper is key to succeeding in this class. This skill can only be developed over time with lots of consistent effort.*

Student response

… during lecture I sit eagerly on the edge of my seat waiting to hear the next answer to the question asked!

… got me excited to learn.

… keep the course interesting by providing a different perspective on the material we read from the textbook.

I really liked the critical thinking this course promoted. Being actively engaged during lecture to think and discuss the material was refreshing and kept the course interesting!

This class was awesome! I love how I am now able to tackle any scientific paper in a few hours, regardless of the subject matter being something I am knowledgeable about or not. I really liked the in-class peer instruction as well, I feel I was able to apply the concepts much better after discussing with my group mates.

The number of papers you read is pretty hefty, but you'll walk away with an understanding of research science and be able to pick up any paper with a frightening title and laugh.

Student response

I wish more bio classes followed this format.

… quenches students' thirst for knowledge!

… intellectually stimulates everyone in class to join in discussion.

… the questions she poses to the class are always thought provoking, making you see and think beyond just mere factoids we have to memorize.

… teaching style really makes it easy to 1) understand during lecture and 2) understand it weeks later.

… encourages students to answer questions and think critically.

… always pushing us to the next level.

… taught in a mentally stimulating way.

… wakes me up and has me ready to learn.

Difficult, but teaches very important critical thinking skills.

… sometimes I wish the class was longer, so we could talk about the topics longer.

… very intellectually stimulating. Also super hard.

This is a HARD class, but incredibly useful.

Student response

I couldn't imagine taking this class in a format other than the one provided by these professors.

Tough with lots of material, but loads of fun and lecture always seems to go by way too fast.

I love the interactive style and makes a huge class feel more like a discussion. I also love how this class was based mostly on primary literature and learning how to dissect and understand. It is an invaluable tool both as a student of science and for learning to think critically in general.

… very rewarding since you learn to read and decipher research papers.

You will learn a lot and you can see yourself grow in the course.

It was very fun and interesting. Reading journal articles are difficult but you feel like you accomplished a lot through this class. Now reading papers are not as terrifying and I can actually understand!

One of the most difficult biology courses on campus. It takes a lot of work and effort in order to succeed in this class, but it is definitely rewarding and you pick up a lot of valuable analytical and research paper reading skills. It's also one of the best biology courses offered at UCSD.

Student response

I'm not sure I will remember the details of the pathogens we learned about, but I definitely think my reading comprehension and critical thinking skills were challenged and have improved over the course of this class.

The section papers really help me in other courses that require that I read scientific papers. I'm really surprised on how much I've gained in scientific paper literacy!

Papers were interesting, I really liked how a paper would seem like complete gibberish, and then three hours later, I would be speaking to others about the paper and feel like an expert in the field. I was amazed how much faster I am able to read scientific papers now as compared to before this class. I had experience reading scientific papers in my lab, but never to this extent. Loved it!

Student objections

too stressful

too much reading

not enough time to click in after discussion

reading comprehension questions too hard